HISTO PATHOLOGICAL ANALYSIS OF CENTRAL NERVOUS SYSTEM NEOPLASMS WITH IMMUNOHISTOCHEMICAL CORRELATION

DISSERTATION

SUBMITTED FOR M.D BRANCH III

[PATHOLOGY]

MARCH – 2010

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI – TAMILNADU

CERTIFICATE

This is to certify that this dissertation entitled **" HISTO PATHOLOGICAL ANALYSIS OF CENTRAL NERVOUS SYSTEM NEOPLASMS WITH IMMUNOHISTOCHEMICAL CORRELATION"** is the bonafide record work done by Dr. Velayutham Sumathi submitted as partial fulfillment for the requirements of M.D Degree Examination Pathology to be held in March 2010.

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ACKNOWLEDGEMENT

I wish to express my sincere and profound gratitude to my **PROFESSOR Dr.N.ARUMUGAM, M.D.,** Professor and Head of the Department of Pathology, Thanjavur Medical College, Thanjavur, for his valuable guidance at every stage, constant encouragement and words of advice which have been the motivating forces in bringing forth this piece of work.

I am also extremely grateful to **Dr. M. SARASWATHI, M.D & Dr.A.L. SHANTHI, M.D.,** Associate professors of pathology who have offered many valuable suggestions and encouragement during this period, whose help has been invaluable to me.

My heartful thanks to Dr**. A. VASAHAR, M.D.,** Associate professor for his valuable guidance and encouragement throughout my study.

I am also thankful to all my Assistant professors for their valuable suggestions and guidance at every stage in this study.

I would also like to express my sincere thanks to my fellow-postgraduates, Lab technicians and all the staffs of the department for their generous help throughout my study.

Above all, I thank our DEAN, for granting me the permission to carry out this work.

A Dissertation on

"ORAL CLONIDINE AS A HYPOTENSIVE AGENT IN FESS SURGERY"

Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirement
For the award of degree of

M.D. BRANCH X
(ANAESTHESIOLOGY)

DEPARTMENT OF ANAESTHESIOLOGY
STANLEY MEDICAL COLLEGE
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI

MARCH 2008

ACKNOWLEDGEMENT

I wish to express my sincere thanks to **PROF. DR. MYTHILY BASKARAN, DGO, MD, DEAN**, Govt. Stanley Medical College and Hospital for having kindly permitted me to utilize the facilities of the hospital for the conduct of the study.

My heartfelt thanks to **PROF. DR. R. MEENAKSHI, M.D. D.A., Prof. & HOD,** Department of Anaesthesiology, Govt. Stanley Medical College and Hospital for her motivation, valuable suggestions, constant supervision and for providing all necessary arrangements for conducting the study.

My sincere thanks to **Prof. Dr. JACINTH CHELLAIAH, M.S. (ENT) DLO, Prof. & HOD,** Department of Otorhino-laryngology, Govt. Stanley Medical College and Hospital and his faculty for their kind co-operation and support.

I am greatly indebted to **Prof. Dr. ESTHER SUDHARSHINI RAJKUMAR, M.D., D.A., Prof. Dr. GANTHIMATHY, M.D., D.A., Prof. Dr. B. KALA, MD.DA., Prof. Dr. S. GUNASEKARAN, M.D., M.D., D.A., DNB,** for their expert guidance throughout the study.

I owe a lot to My Assistant Professors **Dr. P. MAHENDRAN** and **Dr. JEGAN MOHAN,** who were guiding me throughout the study and supervising periodically.

I thank **ALL ASSISTANT PROFESSORS** who evinced keen interest and gave support without which this study would not have been possible.

I thank **Mr. PADMANABHAN,** Statistician, for helping me in the statistical analysis.

I thank all the post graduates for their valuable support during the study period.

I thank all the theatre personnel for their co-operation.

I thank all the patients, without whose participation this study would not have been possible.

CONTENTS

INTRODUCTION

The central nervous system [CNS] is made up of the brain and the spinal cord. Cells within the CNS normally grow in an orderly and controlled way. If for some reason this disorder is disrupted the cells continue to divide and form a lump of tumor.

Primary brain tumors continue to be among the top ten causes of cancer related deaths in the world, despite comparatively low incidence to other tumors. Approximately 14/1,00,000 people are diagnosed with primary brain tumors each year and 7/1,00,000 are diagnosed with primary malignant brain tumors. About half to three quarters are primary tumors, rest are metastatic.

Tumors of CNS account of 20% of all cancers of childhood. The incidence of brain tumors is 2-5 new cases per 1,00,000 per year. 70% of childhood tumors arise in posterior fossa, a comparable number of tumors in adults arise within cerebral hemispheres above the tentorium.

CNS brain tumors is about equal in males and females – 51% for females and 49% for males (CBTRUS STUDY). The incidence of malignant CNS tumors is greater in males i.e. 7.2/1,00,000. Brain tumor incidence tends to be higher in countries with more developed medical care.

Research into the causes of brain tumors is mired by many factors, including the relative rarity of the disease and rapid death of patients with aggressive subtypes. Investigators have initiated studies of genetic polymorphisms that when coupled with certain environmental exposures may lead to brain tumors. The possible risk of developing brain cancer from exposure to electromagnetic fields through power lines has been investigated. To date, studies do not support any such relationship. Another area of popular concern is the possible association between head trauma and brain tumor development.

Central Nervous System tumors have unique characteristics that set them apart from neoplastic processes elsewhere in the body.

1. Distinction between benign and malignant neoplasm is less evident in CNS than in other organs.
2. The ability to resect infiltrating glial neoplasms surgically without compromising neurologic function is limited
3. Anatomic site of neoplasm can have lethal consequence irrespective of histologic classification.
4. Pattern of spread of primary CNS neoplasms differ from that of other tumors, even the most highly malignant gliomas rarely metastasise outside the CNS.

Glial tumors are the most common primary brain tumors. They are derived from astrocytes, oligodendroglial cells and ependyma. Metastatic tumors are by far the commonest group of malignancies encountered within nervous system. Bronchus, breast and bowel are the most common primary sites but metastases can develop from almost anywhere.

Recently there has been conjecture that primary brain tumor incidence is increasing. Analysis of the speculation is complicated by diagnostic discrepancies and ascertainment bias in registry data. However after extensive review this apparent rise is most likely caused by factors such as better diagnostic procedures, improved access to medical care and enhanced care for the elderly – all leading to greater detection rather than an actual increase in incidence.

Sometimes CNS tumors are very difficult to diagnose under light microscopic examination. Immunohistochemical stains play an immense role in differentiating these tumors.

In this prosepective study of CNS tumors, incidence with respect to age, sex, site and histomorphological features of various tumors are studied with an immunohistochemical correlation for some tumors where light microscopic examination was difficult.

The recent literature regarding CNS tumors are also reviewed and correlated.

REVIEW OF LITERATURE

Tumors of the central nervous system are a heterogeneous group of neoplasms exhibiting a variety of histological features and cytological characteristics. Oncogenetically only cells with proliferative capacity in the CNS can produce tumors.

About 60% of primary intracranial neoplasms are gliomas. 20% are Meningiomas and the remaining 20% are shared by other tumors. Paediatric CNS neoplasms tend to be infratentorial whereas in adults they are mainly supratentorial.

Classification and Grading of CNS tumors

Baily and Cushing (1926) were pioneers in the histological typing of glial tumors. The evaluation of the tumor tissue focused on the resemblance of adult glioma cells with cells at various stages of embryogenetic differentiation. Kernohan and Sayre (1952) favored a more simplified classification system, which subdivided gliomas into astrocytomas, Oligodendrogliomas and ependymomas on the basis of cell differentiation.

Astrocytic tumors comprise a number of cytological and histological varieties (Vandenberg 1992, Kleihues et al. 1993a). One fundamental subdivision has been made between diffuse astrocytomas, Pilocytic astrocytomas, Pleomorphic xanthoastrocytomas and subependymal giant cell astrocytomas (Kleihues et al.

1993b). The latter three tumors generally represent a more circumscribed growth and favorable prognosis. Diffuse astrocytomas show a growth pattern that infiltrates the surrounding tissue. The tumor entity has been termed as the diffusely infiltrating astrocytomas. They are the most common of the astrocytic lesions and encompass three histological variants: the fibrillary type, the protoplasmic type and the gemistocytic type. The fibrillary type is the most typical variant. Gemistocytic differentiation, also as a composition, has been associated with a relatively rapid tumor progression, whereas protoplasmic astrocytomas have been shown to represent a more benign tumor behaviour (Watanable et al. 1997 prayson and Estes 1996).

Grading of CNS tumors

Numerous grading systems have been defined for astrocytomas, most use the 3 or 4 tier grading system. Currently employed grading systems are WHO grading system and the St.Anne Mayo.Grading system. Histological criteria taken into consideration are nuclear atypia, mitosis, micro vascular proliferation and / or necrosis.

Thus astrocytoma with none of the above histological features is graded as grade I

Nuclear atypia - grade II

Nuclear atypia + Mitosis - grade III

Nuclear atypia + Mitosis + Micro vascular proliferation and/or Necrosis-grade-IV

WHO uses Roman numericals, whilst St. Anne Mayo uses Arabic numericals the only difference is that in WHO systems, tumors such as pilocytic astrocytoma, subependymal giant cell astrocytoma are accepted as grade 1 tumors.

Currently the malignancy scale of WHO classification and the St. Anne Mayo grading system have proved to be both highly reproducible and predictive of patient survival.

Patient's survival also depends on a variety of clinical parameters including patient's age, clinical condition, tumor location and treatment e.g. Extent of surgical resection, postoperative radio and/or Chemotherapy.

Despite these variables, typical ranges of survival are more than 5 years for low grade diffuse astrocytoma, 2-5 years for anaplastic astrocytoma and less than 1 year for Glioblastoma. The WHO grading system is applicable to all other CNS neoplasms. Among the other neuroepithelial tumors Oligodendrogliomas are graded as II & III. All primitive Neuroectodermal Tumors and primary CNS germ cell tumors are graded as IV, but unlike glioblastoma, they have a better mean survival time since most are radio or chemo sensitive neoplasms.

Comparison of the World Health Organization (WHO) and St.Anne/Mayo grading system of astrocytomas.

WHO Grade	WHO designation	St. Anne / Mayo Designation	Histological criteria
I	Pilocytic astrocytoma	-	-
II	Diffuse Astrocytoma	Astrocytoma grade II	One criterion, usually nuclear atypia
III	Anaplastic Astrocytoma	Astrocytoma grade III	Two criteria, usually nuclear atypia and mitotic activity
IV	Gliblastoma Multiforme	Astrocytoma grade IV	Three criteria: nuclear atypia, mitosis,endothelial proliferation and/or necrosis

Diagnosis of CNS tumors is assisted by the use of specialised histochemical stains for glial cells, neurons and other CNS elements. These techniques however, have been largely replaced by the more sensitive and specific immunohistochemical methods. For glia the cajal gold chloride sublimate method has been replaced with the glial fibrillary acidic protein (GFAP) immunostaining and the Bielscowsky silver impregnation for neuronal elements by immunostaining using antibody to synaptophysin, neurofilament protein and microtubule associated protein. Use of the phosphotungstic acid hematoxylin (PTAH) technique for glial processes has been largely retained. For vascular tumors special stains like Masson's trichrome, Verhoffs and reticulin are used.

The staining for the glial fibrillary intermediate filament is present in normal, reactive and neoplastic astrocytes (paetau 1989, burger et al, 1991). GFAP expression in astrocytoma has been shown to decrease along with the differentiation process (Schiffer et al, 1986). Other routinely used immunohistochemical staining in brain tumor diagnosis include in alphabetical order carcino-embryonic antigen (CEA,positive example in metastatic carcinoma), chromogranin (Neuroendocrine tumor), cytokeratin (CK, metastatic carcinomas), epithelial membrane antigen(EMA, meningiomas), HMB-45(melanomas), Leukocyte common antigen (LCA, lymphomas), Placental alkaline phosphatase (PLAP, germcell tumors), S-100(Schwannomas), and synaptophysin (primitive neuroectodermal tumors) (Ackerman 1996).

Glial fibrillary acidic protein (GFAP) is an intermediate filament specifically expressed in glial cells. This marker is a major constituent of glial cytoplasmic filaments, which helps to maintain and stabilize the glial cytoskeleton. It is present in normal, reactive, neoplastic astrocytes, ependymal cells, developing and neoplastic oligodendrocytes.

Synaptophysin (SYN) a component of synaptic vesicle membrances expressed in normal neuropils in the gray matter and neoplastic well-differntiated neurons. It is negative in normal, reactive and neoplastic glial cells.

Fibrillary astrocytoma

Low-grade astrocytomas represent only a small proportion of astrocytic tumors or gliomas in general. The reported proportions vary [8,37,43,54,59] at Newyork university (NYU) Medical center in the period 1977 thro 1998. Only 53 examples were found in a retrospective review of more than 1500 adult gliomas in the neuropathology files.

Sites:-

Grade I/III fibrillary astrocytomas are most common in the cerebral hemispheres (60% of pediatric examples) . In the cerebellum, diffuse low grade cerebellar tumors recur more frequently than their pilocytic counterparts[17.26], overall the survival and functional outcome associated with cerebellar astrocytomas is excellent [24.32.52]. In contrast, the term brainstem glioma usually is used to describe diffuse high-grade astrocytomas that infiltrate and expand the pons substantially; these tumors are associated with a poor prognosis. [4.5.39.50].

A review of a series of 100 children with intrinsic gliomas of the cord subjected to radical excision at NYU20 yielded 45 low-grade astrocytomas.[35.36]
Gross – Mass lesion, Gray or white Matter with indistinct boundaries, small or large cyst, firmness.

HPE – Mildly cellular tumor composed of fibrillar to stellate cells with minimal nuclear pleomorphism and lacking mitotic activity.

IHC – GFAP Immunoreactive diffusely positive

Gemistocytic astrocytoma

Variant of astrocytoma composed of variable fraction of Gemistocytic neoplastic astrocytes. Gemistocytes should be more than 20% of all tumor cells.

Gemistocytic astrocytoma WHO Grade II or III lesions rapidly progress to globlastoma. [53]

IHC – Constantly express GFAP.

Protoplasmic astrocytoma

Rare variant composed of neoplastic astrocytes showing a small cell body with few flaccid processes, low content of glial filaments and scant GFAP expression.

When occurring in children this neoplasm may be difficult to separate from pilocytic juvenile astrocytoma.

Anaplastic astrocytoma

The peak age at which an anaplastic astrocytoma is diagnosed has been reported to be about 45 years.[9.48] Patients under 40 to 45 years of age do much better than patients over that age, and patients over 60 to 65 do markedly worse than all younger patients.[11.48] .

Gross- Solid tumor exhibiting friable, gray granular tumor tissue merging with the surrounding brain. Marked enlargement of adjacent gyri and basal ganglia HPE – Moderately to highly cellular tumor composed of fibrillar cells with IHC – GFAP – immunoreactive.

Glioblastoma

It represents at least one quarter of all adult gliomas and over 15% of pediatric gliomas (including brainstem examples). In adults, the majority are encountered as cerebral hemispheric masses. Most often apparently centered in

white matter. The peak age for adult patients is about 55 years, which is significantly different from that for the anaplastic astrocytoma. A cerebellar glioblastoma is uncommon in any group. [8.32.59]

Gross- poorly delineated mass c/s – variegated appearance of red, brown, blacks, gray and white reflects hemorrhage. necrosis and expansion, often multifocality. Blurring of tumor/brain interfaces and gray white junctions obliterated by neoplastic tumors and associated edema.

HPE – Markedly cellular tumor composed of highly anaplastic pleomorphic cells with significant nuclear pleorphism. Vascular proliferation. mitotic activity and necrosis (with or without) pseudopalisading tumor cells.

IHC-GFAP multifocally reactive (may be scanty).

Giant cell Glioblastoma

Gross-well circumscribed. firm. Superficially located in the temporal and parietal lobes

HPE- Glioblastoma with numerous multinucleated giant cells, small fusiform syncytial cells and reticulin network.

IHC – GFAP expression is highly variable.

Gliosarcoma

Gross – Firm superficial mass

HPE- a biphasic tissue pattern with areas displaying gliomatous or mesenchymal differentiation is essential. Neoplastic mesenchymal appearance and reticulin formation.

IHC- Gliomatous component shows strong GFAP expression, sarcomatous components show reticulin network.

PilocyticAstrocytoma (PCA)

Pilocytic astrocytomas have been recorded from virtually all portions of the brain, but the large majority occurs in the cerebellum (usually in hemisphere) and the hypothalamus and related optic chiasma. cases localized to the deep gray matter (thalamus, basal ganglia, cerebral white matter, brainstem, and spinal cord) are much less common.

Gross-Soft, gray, discrete tumor mass with cyst formation is common

HPE- juvenile pilocytic astrocytic tumor of low cellularity exhibiting a biphasic pattern with bipolar cells, Rosenthal fibers, loose textural multipolar cells, microcysts and granular bodies.

Adult PCA are formed of delicate elongated nuclei with their bipolar hair like fibrillar processes usually arranged in a fascicular pattern. Microcystic areas and Rosenthal fibers are usually absent. They have a less favourable prognosis[6] than the juvenile type because they tend to infiltrate adjacent brain.

IHC – Strong GFAP immunoreactivity highlights cytoplasmic processes.

Pleomorphic Xantho Astrocytoma (PXA)

Gross- PXA are attached to the meninges and accompanied by a cystic mural nodule within the cyst wall.

HPE- Tumor composed of fibrillary and giant multinucleated neoplastic astrocytes. Diagnostic hallmarks are large Xanthomatous cells, dense intercellular reticulin network and lymphocytic infiltration. Eosinophilic granular bodies present.

IHC-GFAP Immunostaining of large plemorphic tumor cells.

Oligodendroglioma

Oligodendrogliomas have incidence of 5 to 15%, the true proportion may be low as 1%.[8.40.59] Most olidendrogliomas are found in the hemispheric white matter.

Gross: -well defined soft masses of grayish pink color. Mucoid degeneration appear gelatinous. Calcification. cystic degeneration, and hemorrhage present.

HPE:- Moderately cellular and composed of tumor cells with rounded homogenous nuclei and on paraffin section a swollen clear cytoplasm

(Honeycomb appearance)

.Micro calcification Mucoid / cystic degeneration and a dense network of branching capillaries, Microgemistocytes present.

IHC: - GFAP positive in mini gemistocytes and gliofibrillary oligodendrocytes, S-100 – diffuse and strong immuno reactivity.

Anaplastic Oligodendroglioma:-

Gross: - Masses of Grey pink color, mucoid and cystic degeneration, calcification present.

Hemorrhage and areas of necrosis seen.

HPE: - An oligodendroglioma with focal or diffuse features of malignancy such as increased cellularity, marked cytological atypia and high mitotic activity. Microvascular proliferation and necrosis may be present. Gliofibrillary oligodendrocytes and minigemistocytes are frequent.

Oligoastrocytoma:-

Gross: - Well defined soft masses of grayish color. Mucoid degeneration appear gelatinous. Calcification, cystic change and hemorrhage present.

HPE:- A tumor composed of mixture of two distinct neoplastic cell types with micro calcification and microcystic degeneration present. It may be divided into biphasic and intermingled variants. It is important to differentiate between oligoastrocytoma and pure astroglial tumors because oligoastrocytoma responds to polychemotherapy.[53]

IHC: - GFAP and vimentin expression are more consistently found in the astroglial component compared with a more variable expression in the oligodendroglial tumor cells.

Anaplastic Oligoastrocytoma

Gross: - Masses with foci of necrosis and hemorrhages, cystic degeneration and calcification.

HPE: - Oligoastrocytoma with histological features of anaplasia.

Ependymoma

In most large series, ependymomas are rather rare brain tumors, comprising fewer than 5% of all gliomas [46.56.59] . They are considerably more common in children, however, they represent almost 10% of gliomas[14.21] and rank third behind

PNET's and astrocytomas in frequency. Spinal cord gliomas are uncommon, but among them the ependymoma is unusually prominent in adults. Ependymomas are likely to be the most common type of intramedullary spinal cord tumor.-[15.46.56]

Gross: - Well demarcated, soft, grayish red tumor, necrosis and hemorrhage present.

- In the spinal cord – Well defined, homogenous and granular tumor.

HPE: - moderately cellular gliomas with a monomorphic nuclear morphology. Key histological features are perivascular pseudorosettes and ependymal rosettes. Myxoid degeneration, hemorrhage, calcification, occasionally foci of cartilage and bone formation.

Variants : - Cellular ependymoma. Papillary ependymoma. Clear cell ependymoma and tanycytic ependymoma.

IHC : - GFAP is typically weak throughout the tumor, with prominent pseudorosettes.

Anaplastic Ependymoma

In Children, fourth ventricular ependymomas are notorious for being refractory to therapy and producing a fatal outcome. Supratentorial ependymomas in children carry a similar poor prognosis. In adults, surgical resection of spinal cord ependymomas is often curative and cerebral hemispheric tumors may have a prolonged and relatively favourable course because of their ready access to

ventricular spaces. Thus ependymomas have some capacity to metastasize in the CSF to distant neuroaxial sites.

HPE : - Ependymoma shws features of anaplasia.Perivascular rosettes are a histological hall mark but ependymal rosettes are absent.

IHC : - Immunoreactivity resembles those of conventional ependymoma but GFAP expressions may be reduced.

Myxopapillary ependymoma

These tumors have a substantial incidence of CSF metastasis,but they are rarely fatal.[62]

Gross: - Encapsulated, lobulated soft and grayish appearance.

HPE : - Typically a papillary tumor with exaggerated myxoid change around blood vessels. Often exhibits long fibrillar process projecting through mucinous material to blood vessels.

IHC : - GFAP typically weak through out the tumors with perivascular area exhibiting strong fibrillary reactivity.

Subependymoma :

Gross : - Firm nodules of variable size bulging into ventricular lumen.Well demarcated tumor.

HPE : - Characterised by cluster of isomorphic nuclei embedded in a dense fibrillary matrix of glial cell processes with small cyst. Mitosis absent.

IHC : - GFAP variable immunoreactive.

Choroid Plexus Papilloma :

Gross : - Circumscribed cauliflower – like masses that may adhere to the ventricular wall. but are well demarcated from the brain tissue.

HPE : - Well differentiated papillary neoplasms in which cuboidal cells arranged in a single layer on thin delicate papillary fronds. No mitosis.

Choroid Plexus Carcinoma :

Gross : - Solid invasive tumor with hemorrhage and necrosis

HPE : - Dysplastic cytological features including increased nuclear to cytoplasmic ratio, mitotic activity, pseudostratified appearance and loss of basal nuclear polarity. Also exhibits cellular invasion into cerebral parenchyma with sheet like growth pattern.

IHC : - Cytokeratin, Vimentin . S – 100 + ve & GFAP focally Positive.

Chordoid Glioma of third ventricle :

HPE : - composed of clusters and cords of epithelial cells within a mucinous stroma.

Stroma contain lymphoplasmacytic infiltration.

Gliomatosis Cerebri.

Gross : - Neoplastic growth and enlargement of involved structures without any mass.

Micro - Elongated glial cells with hyperchromatic oval nuclei and increased mitotic activity.

IHC – GFAP , S – 100 Positive.

Neuronal & Mixed Neuronal – Glial Tumors.

Ganglioglioma & Gangliocytoma :-

Gross – Solid / Cystic tumor, no mass effect , calcification present.

Gangliocytoma HPE : - Irregular groups of large multipolar neurons that show dysplastic features. Stroma shows reactive glial cells and network of reticulin fibers.

Ganglioglioma HPE : - Additional neoplastic glial component surrounded by a reticulin network.

Desmoplastic Infantile Ganglioglioma :

Gross : - Large tumor involving superficial cortex and leptomeninges often attached to dura.

HPE : - Desmoplastic stroma with entrapped astrocytes and / or neuronal cells.

IHC – Glial cells express both GFAP and vimentin while neuronal differentiation is disclosed by synaptophysin.

Dysembryoplastic neuroepithelial tumor

Gross : - Intracortical , multinodular firm mass.

HPE : - Typical glioneuronal element comprising microcystic spaces, oligodendrocyte like cells and floating neurons often associated with cortical dysplasias.

Central Neurocytoma :

Gross : - Greyish and friable intraventricular tumor and calcified areas.

HPE : - Small regular polyhedral cells with honey comb like arrangement, round regular nuclei and pale cytoplasm. Micro calcifications are common.

Pineal tumors

Pineoblastoma :

Gross : - Soft, friable, poorly demarcated tumor, hemorrhage and / or necrosis may be present.

HPE : - pineoblastomas are composed of pattern less sheets of densely packed small cells with round to irregular nuclei and scant cytoplasm. Pineocytomatous rosettes are lacking , but Homer – Wright and Flexner – wintersteiner rosettes may be seen.

IHC : - Synaptophysin , Neuron Specific Enolase (NSE) and Chromogranin positive.

Pineocytoma : -

Gross : - Well circumscribed lesions, grey tan in colour.

HPE : _ Composed of small uiniform mature cells resembling pineocytes. It grows primarily in sheets and also shows features of large pineocytomatous rosettes composed of abundant delicate tumor cell processes.

IHC : - Synaptophysin , NSE & Neurofilament positive.

Embryonal tumors

Medulloepithelioma :

Gross. – Well circumscribed tumor with areas of necrosis and hemorrhage.

HPE : - Characterised by papillary, tubular / trabecular arrangement of neoplastic neuro epithelial cells with an external limiting membrane.

IHC : - Nestin positive which is confined to the basal area.

Ependymoblastoma :

Gross : - Well circumscribed distinct tumor margin

HPE : - Central primitive neuro ectodermal tumors with multilayered rosettes in which cells in the outer rim of the rosettes merge with the surrounding undifferentiated neuroectodermal cells.

IHC : - S – 100 , Vimentin, Cytokeration and GFAP Positive.

Medulloblastoma (MB)

Gross : - Circumscribed firm discrete mass.

HPE : - densely packed cells with round to oval or carrot shaped hyperchromatic nuclei surroundred by scanty cytoplasm. Neuroblastic rosettes which consist of tumor cell nuclei disposed in a circular fashion around tangled cytoplasmic processes are typical.

IHC : - Typically synaptophysin positive, GFAP positive rarely seen . S – 100 variable.

Variants – Desmoplastic MB . MB with extensive nodularity, Large cell MB , Medullomyoblastoma. Melanotic MB.

Supratentorial primitive neuroectodermal tumor (PNET)

Gross : - The parenchymal tumors may be massive growths with or with out cysts and hemorrhages. Demarcation between the tumor and the brain may range from indistinct to clear.

Cut surface show soft. pinkish color.

HPE : - are composed of undifferentiated or poorly differentiated neuroepithelial cells which may vary in their morphological features Cerebral suprasellar PNETs are basically similar to medulloblastoma.

Atypical teratoid/rhabdoid tumor

Gross – Soft pinkish red bulky neoplasm, hemorrhage and necrosis present.

HPE – Rhabdoid cells with variable components of primitive neuroectodermal component.

Mesenchymal and epithelial cells present.

IHC – GFAP, Synaptophysin, EMA, Cytokeratin and NSE immunoreactive.

Tumors of central and peripheral nerves.

Schwannoma

Gross – Globoid masses few cm to 10 cm in size.

c/s Light tan glistening tissue interrupted by bright yellow patches.

HPE-Tumor composed of spindle shaped neoplastic schwannian cells with alternating areas of compact elongated cells with nuclear palisading (Antoni A) and less cellular, loosely textured areas (Antoni B) palisading tumor cell nuclei called verocay bodies.

Variants – Cellular. Melanotic and Plexiform.

IHC-S-100 positive. Leu – 7 positive.

Neurofibroma

Gross – fusiform well circumscribed tumor

c/s – firm glistening and grey-tan

HPE – Composed of neoplastic Schwann cells, perineuronal like cells and fibroblast in a matrix of collagen fibers.

IHC-S-100 Positive.

Malignant peripheral nerve sheath tumor

Gross-Globoid pseudoencapsulated tumor, firm to hard

c/s Grey with foci of necrosis and hemorrhage.

HPE-Typically a fibrosarcoma like fasciculated growth of tightly packed hyperchromatic spindle cells with abundant faint eosinophilic cytoplasm.

Variants-Epitheloid, Glandular, Malignant Triton tumor.

Meningeal tumors

Cushing and Eisenhartdt, in their classic two volume monograph on meningiomas that was published in 1938, cited the prevalence of meningiomas as 13.4% of all intracranial tumors. The overall incidence of meningiomas reported in the literature ranged from 1 to 2.8 per 100.000 persons.[58]

Meningiomas in children are rare The hospital for sick children in Toronto reported an incidence of 13 meningiomas among 1283 intracranial tumors and an average age at presentation of 11.6 years. The female predominance of meningiomas seen in adults is absent in childhood.[19] Studies in which CT or MRI was used revealed a peak incidence in the seventh decade of life[58]. In a recent autopsy series, the percentage of incidentally discovered meningiomas increased as age increased and was highest in people older than 80 years.[47]

Malignant meningiomas tend to recur after complete resection at a much higher rate (70% within 8 years) than that of benign meningiomas (up to 20% within 10 year).[45,58] The extent of surgical resection is the critical determinant of survival[45].

Extra cranial metastasis from a meningioma is rare (0.1% of cases) but occurs more frequently in particular subtypes (e.g., 30% of papillary meningiomas metastasize).[23] Sites of metastasis in decreasing order of frequency are as follows: lungs / pleura, musculoskeletal system, liver, reticuloendothelial system and kidneys.[63.]

Benign meningioma

Gross-Rubbery or a firm well demarcated rounded mass that have a broad dural attachment.

HPE-Tumor cells form lobules which are surrounded by thin collagenous septae. Cells are uniform with oval nuclei, even chromatin and eosinophilic cytoplasm forming syncytium.

IHC-EMA positive

Atypical meningioma

Gross-Large tumor with cystic change

HPE-Sheeting pattern of tumor cells, brain invasion, necrosis, nuclear pleomorphism, prominent nucleoli and increased mitotic activity.

Malignant meningioma

HPE-features of atypical meningioma with increased mitotic activity.

IHC – EMA positive, Vimentin, S-100 positive, CEA and cytokeratin positive.

Hemangiopericytoma

Gross-Solid well demarcated tumor, tendency to bleed during surgery.

Cut surface fleshy grayish to red brown.

HPE-Highly cellular monotonous tumor composed of plump cells with scant cytoplasm accompanied by numerous small vascular spaces and dense network of reticulin fibers.

IHC-Vimentin and factor 13A positive.

Malignant lymphoma

Gross-Single or multiple masses in the cerebrum, firm friable gray yellow with central necrosis.

HPE-Lymphoma that diffusely infiltrates the brain parenchyma in an angiocentric pattern forming collar of tumor cells within concentric perivascular reticulin deposits.

Variants –B-cell lymphoma. T-cell lymphoma. Plasmacytoma. Angiotrophic lymphoma, Hodgkin disease, MALT lymphoma of dura.

Germ cell tumors

Germinoma-Solid, soft, friable, tan white tissue

IPE-Composed of uniform cells resembling primitive germ cells with large vesicular nuclei, prominent nucleoli and lymphoplasmacytic cellular infiltrations.

Teratoma

Gross-Mucous laden cysts, fat, chondroid nodules or bony spicules, Rarely well formed hairs or teeth.

Mature teratoma

Composed of fully differentiated adult type tissue elements arranged in a pattern resembling normal tissue.

Immature teratoma

Composed of incompletely differentiated components resembling fetal tissues.

Yolk sac Tumor

Composed of primitive appearing epithelial cells set in a loose, variably cellular and myxoid matrix resembling extra embryonic mesoblast. Eosinophilic hyaline globules.

IHC-immunoreactive for AFP

Embryonal Carcinoma

Composed of large cells that proliferate in cohesive sheets and nest, form abortive papillae or gland like spaces. Tumor cells replicate the structure of the early embryo forming embryoid bodies.

Choriocarcinoma

Gross-extensive hemorrhagic necrotic tissue

HPE-Characterized by extra embryonic differentiation along the trophoblast.

Diagnosis requires the identification of cytotrophoblastic elements and syncytio trophoblastic giant cells.

Tumors of Sellar region

Craniopharyngioma

Gross-Well demarcated solid tumor with cystic component, calcification, cyst contains cholesterol rich, machine oil like, thick brownish yellow fluid.

HPE-Consist of strands of ameloblastic epithelium with peripheral palisading of nuclei. Diagnostic features are nodules of compact wet keratin and dystrophic calcification.[53]

IHC-High Molecular Weight Keratins and Low Molecular Weight Keratins positive.

Pituitary adenoma (tumor of the adenohypophysis)

Gross-Well circumscribed, with soft consistency.

Cut surface shows-grey to yellow homogenous or granular

HPE-Consist of densely packed polygonal cells with abundant cosinophilic granular, PAS-positive cytoplasm.

For practical purposes pituitary adenomas may be divided into endocrine-active and endocrine-inactive tumors.[59,66]

Metastatic tumors of the CNS

Gross-Discrete round or well circumscribed grey white or tan masses. Tumors attached to the dura or leptomeninges may form nodules. Hemorrhage may be seen.

HPE-Metastasis are similar to those of the primary tumor from which they arise. Tumor necrosis is frequent with well-defined borders with the adjacent parenchyma and displace, rather than infiltrating the tissue as they enlarge.

Brain tumors can be diagnosed by CT scan and MRI images.

Cell proliferation markers

The cell proliferation markers are – Bromodeoxyuridine (BrdUL). Ki67 and Proliferating cell nuclear antigen (PCNA). Out of these BrdUL and Ki67 are more consistent and their results can be correlated with each cycle. These two antibodies give a fairly good idea about the cell cycle.

The above two markers correlate well with tumor grade and survival. Higher the value of these two antibodies, worse is the prognosis. The interpretation of any immunohistochemistry results should always be done in accordance with the morphology and proper clinical and radiological correlation.

AIM OF THE STUDY

Specimens were studied to find out:-

1. The incidence of CNS neoplasms.
2. To evaluate the anatomical distribution of CNS neoplasms.
3. To evaluate the histopathological features with light microscopy and special stains.
4. To grade the CNS neoplasms according to guide lines provided by the World Health Organization [WHO].
5. To evaluate the role of immunohistochemical markers in CNS tumors for confirmation and arriving at final diagnosis.

DISCUSSION

In this prospective study of CNS neoplasms which covered 83 cases during March 2007 – March 2009, the overall incidence of CNS neoplasms encountered by others was less than 9% (CBTRUS data) and in my observation it was 9.97%

Incidence of various CNS neoplasms is compared with the central brain tumor registry of United States. (CBTRUS study) 2004 – 2005 which is exhibited in the following table.

	Astrocytoma	**Oligodendroglioma**	**Ependymoma**	**Meningioma**	**Neural Tumors**	**Craniopharyngioma**
CBTRUS Study	41.2%	3.2%	2.3%	24%	6.5%	0.9%
Recent Study	41 Cases 49.3%	1 Case 1.2%	1 Case 1.2%	15 Cases 18.1%	7 Cases 8.4%	2 Cases 2.4%

Our study in accordance to CBTRUS study[14] shows that astrocytomas still remain to be the commonest CNS neoplasm (49.3%) followed by meningiomas 18.1%. This table also illustrates that nerve sheath tumors are common neoplasms found in our set up with a slightly higher incidence of 8.4%

Brain tumor incidence tends to be higher in countries with more developed medical care. Although there is no population that is not at risk for developing glioma there is some correlation between incidence and characteristics

such as age, gender, ethnicity and geography according to Nicholas A Butoneski & Susam M. Chang et al[43]

This study shows that CNS Neoplasm are commonly seen between the age groups 31 – 40 yrs (30.1%) followed by 41 – 50 Yrs (21.6%). CNS neoplasms are least commonly seen in the elderly age group i.e between 61 – 70 yrs (3.6%). This was in accordance with the study of Paul - Kleihaus et al [47] In contrast to the same associates who said that CNS neoplasms were slightly higher in males (1.8: 1), our study revealed a slightly higher incidence in females 46 cases (55.4%).

The commonest site of CNS neoplasm in this study occurred in the parietal lobe 27 cases - (32.5 %) followed by frontal lobe 25 cases (30.1 %).

Grading is done for all CNS neoplasms according to the World Health Organisation norms. Grading follows the same guidelines with the Daumas Duport grading system as quoted by Roger. E. Mc Lendon et al.[53]

In this system, one point is accorded to the presence for each of nuclear pleomorphism, mitotic activity, vascular proliferation and necrosis.

zero or 1 point correlates with WHO grade II
2 points correlates with WHO grade III
3 – 4 points correlates with WHO grade IV

While cellular density is not considered in grading, cellular density is a consideration in establishing a diagnosis of neoplasia in the sense that the formation of a tumor is derived solely through the uncontrolled replication of cells. According to the study of Peter et al. [50], the incidence of various CNS neoplasms according to age show

Grade II – 3rd to 4th decade
Grade III – 5th decade
Grade IV – 6th decade

Our study showed that grade I neoplasms were in accordance with the above study whereas grade II and grade IV neoplasms in contrast were seen in 3rd and 5th decades respectively.

Sex wise ratio showed that females outnumbered males in grades I, II and IV whereas grade III neoplasms were predominated by males.

Comparative analysis of incidence of glial tumors studied at various institutions in India with our study was done [41].

S.No	**Study**	**Astrocytoma**	**Glioblastoma**	**Medulloblastoma**	**Oligodendroglioma**	**Ependymoma**
1	Tata Memorial Hospital, Mumbai	46.3%	21.5%	11.1%	6.3%	6.8%

2	Kidwai Memorial Institute of Oncology, Bangalore	41.1%	22.95%	11.2%	9.6%	1.92%
3	Cancer Institute , Adayar, Chennai	39%	29.05%	5.9%	4.4%	3.4%
4	Regional Cancer Institute, Trivandrum	41.35%	13.3%	12.7%	3.35%	2.1%
5	Assam Medical College, Dibsugarh	46.75%	7.1%	8.1%	9.1%	7.1%
6	Present Study	49%	9.6%	4.8%	1.2%	1.2%

The above table shows that astrocytomas constitute the major chunk of gliomas in our study consistent with studies conducted by other institutions(41 cases – 49%).

Of the 41 cases of the astrocytomas diagnosed there were 3 cases of grade I astrocytoma with an incidence of 7.3%. All the three cases, showed only an increase in cellularity. The three cases occurred in the middle age group with a slight increase in males (2:1).

According to the studies of Paul Kleihaus et al.[47] diffuse astrocytomas is the commonest of all astrocytomas, commonly occurring in the middle age group. Our study too showed consistent features (16 cases – 39.02%) with diffuse astrocytomas in the age group of 31- 40 years. According to the same associates, long term follow up studies have shown that with maximum tumor decompression, followed by adequate adjuvant therapies the mean survival of grade II astrocytomas is more than 10 years.

Anaplastic astrocytomas constitutes about 14 cases(34.1%) with peaks between 31 – 40 years and 51- 60 years, according to Paul Kleihaus et al.[47] Mean survival of grade II astrocytomas varied from 2-5 years. Studies of Watanahe. K. Sato et al[62]., showed that the progression of anaplastic astrocytoma to glioblastoma was a key prognostic factor, with a mean of 2 years. Approximately, 10 % of grade III anaplastic astrocytomas show expression of Epidermal Growth Factor Receptor. Cellular proliferation occurs by activation of a tyrosine kinase receptor, platelet derived growth factor and Vascular Endothelial Growth Factor(VEGF). VEGF is involved in the pathways that determine endothelial proliferation and neovascularisation.

Grade IV astrocytomas in the present study, constitute 8 cases(19.5%) of all astrocytomas and 9.6% of all intracranial tumours in contrast to the studies of Zulch KJ et al. [64] who said that glioblastoma accounted 12 – 15 % of all intracranial neoplasms and 50 – 60 % of all astrocytic tumours. 8 cases occurred

in varying age groups peak being between 51 – 60 years, consistent with the studies of Zulch KJ et al. [64] who gives peak incidence between 45 – 70 years. All cases showed necrosis and endothelial vascular proliferation.

Regarding the sex-wise ratio of astrocytomas, our study showed a slight preponderance of males to females. With respect to grades, females outnumbered males in grade II and IV whereas males in grade I and III.

Meningiomas comprised the second largest group of neoplasms in this study with 15 cases constituting 18.1 % of all CNS neoplasms comparable to CBTRUS study[14] and studies done by Lantos PL Vandenberg et al.[30] who gives an incidence of 13.26 % of all intracranial tumors.

All the cases were graded on the basis of WHO norms which included cellularity, pattern, mitosis and necrosis. Out of the 15 cases, 14 cases (93.3%) were diagnosed as grade I meningiomas with varying histological patterns. Features of atypia or anaplasia were not evident in any of the above cases. No atypical meningiomas were seen in the study.

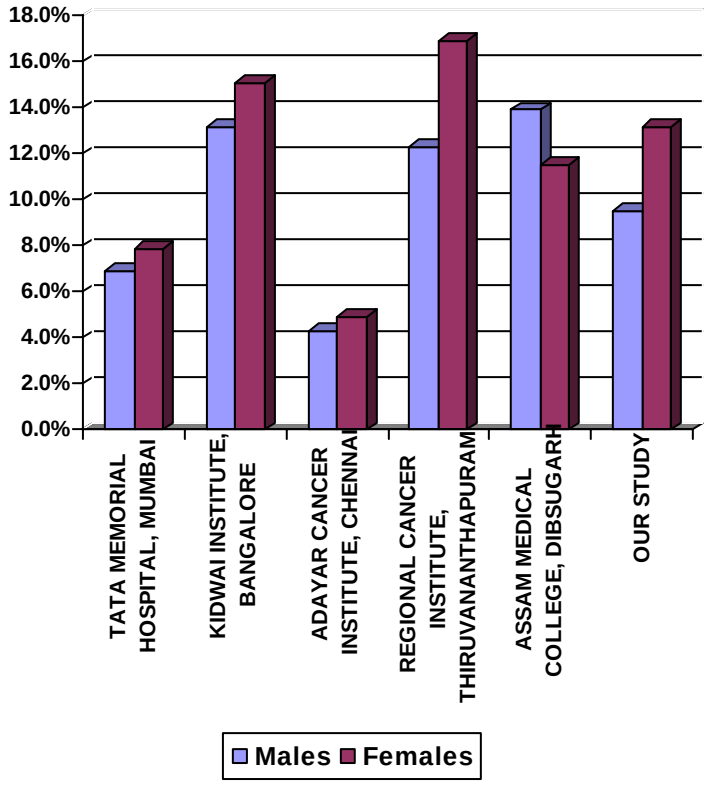
Only one anaplastic meningioma was seen with an incidence of 6.6% of all meningiomas in contrast to the study of Jaerkelainen et al.[28] who gives an incidence of 1 – 2.8%.

According to studies of Paul Kliehaus et al.[47] meningiomas are common in the 6th to 7th decade with a predilection to females. In contrast our study showed a higher incidence of meningiomas between 3rd to 4th decade but were commonly seen in females. [9 cases-60%]. As per the study of Perry. A Stafford et al.[49] meningiomas in children behave very aggressively. In our study there was no such incidence in children.

Neural tumors were the next common group encountered in the present study. As per studies conducted by Cassedi et al. [13] neural tumors constitute 8% of all intracranial tumors with higher incidence in 4th to 6th decade and female to male ratio being 2:1. Our study also showed consistent features with an incidence of 8.4% of all intracranial tumors [7 cases] commonly seen between 3rd to 4th decade with a slight increase in females [4 cases out of 7 – 66%]. Schwannomas were the commonest of neural tumors seen in the study, commonest site of occurrence being the cerebellopontine angle 5 out of 7 cases [71.4%] consistent with the studies of Cassedi et al. [13]

Pediatric Neoplasms

Incidence of pediatric CNS neoplasm was found to be 9 – 10 % by other workers such as CBTRUS study[14] and Rusell DS Rubinstein et al. [55] but in our study it was 13.2%. However the limitation in the present study is the small number of cases encountered in the pediatric age group. Medulloblastoma was the commonest CNS neoplasm in pediatric population seen in our study. Sex wise ratio of pediatric CNS tumors is compared with the studies conducted by various institution in India [41].



Comparative study shows that pediatric CNS neoplasms in other institutions as well as in our study [7 cases-13.2%] are commonly seen in female

children as illustrated in above bar diagram. With respect to grading grade IV neoplasms are frequently encountered in children.

Among the pediatric neoplasms as quoted earlier, medulloblastoma was the commonest neoplasm with an incidence of 4.8% of all intracranial tumors and 36.36% of all pediatric intracranial neoplasms [4/11 cases]. This showed a slight variation with the studies of Mahaley. M. Metilen et al. [36] who gives an incidence of 3% of primary CNS tumors and that of Rutka. J.T et al.,[56] an incidence of 25% of all intracranial neoplasms.

As quoted by Paul Kleihaus et al. [47] medulloblastoma occurs more commonly between 0 -10 Yrs [Peak 7yrs] with a slight predilection in males.

Our study too showed that all the 4 cases seen were less than 10 years but with regard to sex wise ratio, showed an equal distribution.

Medulloblastoma is a highly malignant primary tumor that originates in the cerebellum or posterior fossa. i.e. infratentorial as studied by Coffin GM Braun et al. [15] This feature was consistent with our study which showed that all medulloblastomas originated in the infratentorial region.

The other common neoplasm seen in pediatric population was craniopharyngioma. According to Bunin GR Surawick et al.,[8] craniopharyngioma

constitutes 1.2 – 4.6% of all intracranial neoplasms which was in accordance with our study showing an incidence of 2.4%. In contrast to the same associates who give an incidence of 5 – 10% of all intracranial tumours in children, our study showed a higher incidence of 18.1%. As per studies of Adamson T.E. et al[3], histologically papillary craniopharyngiomas were common in adults and adamantinomatous variant in children. The two cases in our study showed adamantinomatous type of craniopharyngioma consistent with the literature.

We have seen one case of choroid plexus papilloma in the pediatric age group which showed an incidence of 1.2% of all brain tumours and 9.09% incidence in children in contrast with the study of Janish. W. Staneczek et al.[29] who gives an incidence of 0.4 - 0.6% of all brain tumors and 2.4% in children. The site was the ventricle which was consistent with the literature.

The other neoplasm seen in children was oligodendroglioma. As per the study of Paul Kleihaus et al[47], oligodendroglioma was found to be around 6% of all intracranial tumours in childhood with a mean age of 10 years for supratentorial cases. The above observation shows a variation with our study which gives an incidence of 1.2% of all intracranial tumours. The only one case seen was in a female child, site being the supratentorial region.

The other tumor seen was an astrocytoma of grade II with an incidence of 0.9% of all intracranial neoplasms. According to J. Thomas Stocker Louis. P.

Dehner et al.[61] low grade astrocytomas show an incidence of 37% in the pediatric population. Studies of Roger. E. Mc Lendon et al.[53] says that well differentiated fibrillary astrocytoma are unusual in small children and constitutes approximately 30% of all astrocytomas in pediatric age group. Studies done by Paul Kleihaus et al.[47] have suggested an increasing incidence of astrocytomas in children during the past three decades.

Metastatic tumors comprised the next major group of neoplasms in our study. There were 5 cases in our study which gives an incidence of 6.03% of all intracranial neoplasms. All the 5 cases were seen in females between the 2nd and 5th decade. This is in contrast with the studies of Paul Kleihaus et al.[47] who gives an annual incidence of 0.03 to 0.04% with rate of metastasis higher in elderly age group. But the sex-wise ratio was consistent with the literature. The probable site of the primary was known in 3 cases.

The other CNS neoplasms encountered in our study were pituitary adenomas with an incidence of 2.4% which was in contrast with the studies of Cotran Robins et al.[52] who gives an incidence of 10% of all intracranial neoplasms with a peak in 30 – 50 years of age in females. Our two cases were in the age group of 11 – 20 years and 41 – 50 years, with both being in the female population.

In our study we had 4 cases which were difficult to arrive at a diagnosis based on histopathology alone. Hence further evaluation was done with special stains and immunohistochemistry.

The utility of special stains and immunohistochemistry in the diagnosis of CNS neoplasms is well documented.[18] However it is to be noted that results of these specialized staining techniques should be interpreted with caution in the light of findings noted on routine H & E sections.

The present study evaluates the usefulness of special stains like PAS and reticulin in 2 cases, which only has complemented the diagnosis already arrived.

A case of chordoma was seen in our study in a 47 years old male in the right frontoparietal region which was confirmed by light microscopy. A PAS stain was done to demonstrate the presence of mucin in the physalliferous cells.

Reticulin was applied to a case diagnosed as Gliosarcoma / Lymphoma and found that reticulin showed positivity around individual cells. The diagnosis was further confirmed by immunohistochemistry.

Immunohistochemistry was done for problematic cases using a panel of antibodies which is depicted in Table No.22

The case diagnosed as Gliosarcoma / Lymphoma histopathologically showed positivity for GFAP and negativity for CD40, hence a final diagnosis of gliosarcoma was arrived.

2 cases showed positivity for synaptophysin where one was diagnosed as a small cell variant of GBM and another broad diagnosis of SRBCT under light

microscopy, hence arriving at a diagnosis of Primitive Neuroectodermal tumor for both.

Another interesting case was given a spectrum of differential diagnosis as Rhabdomyosarcoma / Malignant Histiocytosis / Lymphoma based on histology. Immunohistochemistry using a panel of antibodies helped in differentiating the three. The above case showed positivity for CD68 whereas negativity for desmin and CD40, left with the diagnosis of Malignant histiocytosis.

MATERIALS AND METHOD

Out of 9629 cases reported totally, 83 central nervous system neoplasm diagnosed clinically were received from Thanjavur Medical College and Raja Mirasudhar Hospital which is affiliated to Thanjavur Medical College. Specimens received during March 2007 to March 2009 are included in this study. Cases diagnosed as neoplasms are included, reactive lesions are excluded from this study.

The specimens received were mostly biopsies as an aggregate ranging from 0.5cc to 5cc. Only 2 specimens, one a case of meningioma measuring 5x4 cms and a case of chordoma measuring 6x4 cms were received. Multiple bits were taken from the tumor masses.

A detailed history with particular attention to clinical symptoms and signs were noted. Site of the tumors were recorded, correlating with the computed tomography findings. A thorough gross examination of the specimens were done.

Histopathological Study of CNS Neoplasms

All the specimens were fixed in 10% neutral formalin and were subjected to histopathological examination. Sections of 3-5 micron thickness were made and routine staining with Haematoxylin and eosin was done.(Appendix I)

Histochemical stains like Reticulin and Periodic Acid Schiff were applied in 2 cases for confirmation. (Appendix II, III)

Immunohistochemistry was done with a panel of antibodies in doubtful cases using Glial fibrillary Acid protein, Synaptophysin, desmin, CD40 and CD 68.(Appendix IV)

OBSERVATIONS AND RESULTS

INCIDENCE :

The annual incidence of CNS neoplasms in our study is 9.97 % (83 cases) which is illustrated in table no .1.

Table-1

Incidence of CNS neoplasms in our study

Period	Total No.of Specimens	Total Neoplasms	CNS Neoplasms	Incidence
March 2007 To February 2008	4956	425	44	10.3%
March 2008 To March 2009	4673	407	39	9.5%
Total	9629	832	83	9.97%

AGE INCIDENCE:

The tumors are grouped according to the age at presentation (ie.1-10 yrs,11 – 20 yrs,21 – 30 yrs, 31 – 40 yrs,41 – 50 yrs, 51-60 yrs and 61 – 70 yrs)

Table -2

AGE & SEX WISE INCIDENCE CNS TUMOURS

Age in Years	Male	Female
1-10	4	6
11-20	2	6
21-30	3	4
31-40	11	16
41-50	10	8
51-60	5	6
61-70	2	1
Total	**37**	**46**

Table.2 (Fig33) shows that CNS tumors occur more frequently in the age group of 31-40 yrs [27 cases,32.5%] followed by 41-50 yrs [18 cases, 21.6%]. Least no. of cases is seen in the age of 61 – 70 yrs [3 cases, 3.6%] followed by 11-20 yrs [8 cases,9.6%] This table also shows a slight preponderance in females [46 cases, 55.4%] whereas males show an incidence of 37 cases - 44.6%.

GRADING :

Grading is done for tumors according to the age based on WHO norms. This includes all CNS neoplasms [neuroepithelial, meningeal, schwannian and embryonal]. This is illustrated in the Table given below.

Table-3

WHO GRADING WITH RESPECT TO AGE GROUP [75 CASES]

Grades	1-10 Yrs	11-20 Yrs	21-30 Yrs	31-40 Yrs	41-50 Yrs	51-60 Yrs	61-70 Yrs
I	3	1	3	11	6	3	1
II	1	2	1	7	6	1	1
II	-	3	2	5	-	4	1
IV	4	1	-	2	3	3	-

Table 3 shows that grade I, grade II and grade III neoplasms are common in the 3rd – 4th decade where as grade IV neoplasms occur in peaks in the Ist decade and 5th to 6th decade. Least no. of tumors are seen in the 6 -7th decade.

Table- 4

INCIDENCE OF CNS NEOPLASMS – WHO GRADE

Grade	No. of Cases	percentage
I	28	37.2%
II	19	25.3%
III	15	20%
IV	13	17.3%

This is followed by table.4 (Fig34) which shows that most of the CNS neoplasms in this study are in grade I [28 cases,37.2%] followed by grade II neoplasms [9 cases,25.3%]. Least no. of cases are seen in grade IV [13 cases,17.3%].

Table-5

GRADING AND SEX WISE INCIDENCE OF CNS NEOPLASMS

Grade	Male	percentage	Female	Percentage
I	10	35%	18	64%
II	8	42%	11	57%
III	11	73%	4	26%
IV	4	30%	9	59%
Total	33	44%	42	56%

Our study show an increased incidence of CNS tumors in females [42 cases,56%] and males [33 cases,44%] which is exhibited in table no.5.(Fig.35). This table also shows that females out number males in grade I [18 cases,64%]. Grade II [11 cases,57%] and grade IV [9case-59%] respectively where as grade III neoplasms are predominated by males [11 cases, 73%].

Table-6 [83 Cases]

INCIDENCE OF VARIOUS CNS NEOPLASMS

S.No	HPE Diagnosis	No A Cases	No of Cases %
1.	Astrocytomas	41	49%
2.	Meningioma (Fig.1)	15	18.1%
3.	Medulloblastoma	4	4.8%
4.	Ependymoma	1	1.2%
5.	Oligodendroglioma	1	1.2%
6.	Craniopharyngioma	2	2.4%
7.	Neural Tumors	7	8.4%
8.	Pituitary Adenoma	2	2.4%
9.	Choroid plexus papilloma	1	1.2%
10	Metastasis	5	6.3%
11	Others	4	4.8%

Table.6 (Fig.36) depicts the incidence of various histological types of CNS neoplasms seen in our study. Astrocytomas constitute the most common neoplasm [41 cases, 49.3%] followed by meningiomas [15 cases, 18.1%], neural tumors [7 cases, 8.4%], metastatic tumors [5 cases,6.03%] and medulloblastomas [4 cases,4.8%]. Least commonly seen tumors in our study are craniopharyngiomas and pituitary adenomas [2 cases each 2.4%] followed by ependymoma (Fig.13), oligodendroglioma and choroid plexus papilloma [1 case each, 1.2%]

Table-7

AGE WISE INCIDENCE OF CNS NEOPLASMS

Grades	1-10 Yrs	11-20 Yrs	21-30 Yrs	31-40 Yrs	41-50 Yrs	51-60 Yrs	61-70 Yrs	Total
Astrocytoma I&II	1	1	3	4	6	3	1	19
Astrocytoma III&IV	-	4	1	7	2	7	1	22
Meningioma I	-	-	2	7	3	1	1	14
Meningioma II&III	-	-	-	1	-	-	-	1
Oligodendroglioma	-	1	-	-	-	-	-	1
Ependymoma	-	1	-	-	-	-	-	1
Medulloblastoma	4	-	-	-	-	-	-	4
Craniopharyngioma	2	-	-	-	-	-	-	2
Pituitary Adenoma	-	1	-	-	1	-	-	2
Choroid Plexus Papilloma	1	-	-	-	-	-	-	1
Deposits	-	-	2	1	2	-	-	5
Schwannoma	-	-	-	4	1	1	-	6
Neurofibroma	-	-	-	1	-	-	-	1
Gliosarcoma/Lymphoma	-	-	-	-	1	-	-	1
Anaplastic Lymphoma	1	-	-	-	-	-	-	1
SRBCT	1	-	-	-	-	-	-	1
Chordoma (Fig.2,22,23)	-	-	-	-	1	-	-	1
Total								**83 Cases**

Table.7 shows the age wise incidence of CNS neoplasms. In the age group of 1-10 yrs medulloblastoma is most common followed by craniopharyngioma. Astrocytoma is the frequently seen neoplasm in the age group of 11-20 yrs and 21-30 yrs. In the age group of 31-40 yrs and above astrocytoma and meningioma are the most commonly seen neoplasms.

Table-8

WHO GRADING FOR ASTROCYTOMAS [41/83 CASES]

S.No	Pathology No	HPE Diagnosis	Increased Cellularity	Nuclear Atypia	Mitosis	Microvascular Proliferation&Necrosis	Grade
1.	99/07	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
2.	188/07	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
3.	300/07	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
4.	471/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
5.	1156/07	Astrocytoma	+ve	-ve	-ve	-ve	I
6.	1204/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
7.	1271/07	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
8.	1636/07	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
9.	1641/07	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
10.	1674/07	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
11.	1721/07	Astrocytoma	+ve	-ve	-ve	-ve	I
12.	1831/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
13.	2172/07	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
14.	2431/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
15.	2489/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
16.	2691/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
17.	2738/07	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
18.	3053/07	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
19.	3085/07	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
20.	83/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
21.	293/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
22.	550/08	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
23.	726/08	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
24.	855/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
25.	874/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
26.	1416/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
27.	1541/08	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
28.	1542/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
29.	1922/08	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
30.	1943/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
31.	2122/08	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
32.	2253/08	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
33.	3063/08	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
34.	3118/08	Glioblastoma Multiforme	+ve	+ve	+ve	+ve	IV
35.	3133/08	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
36.	3516/08	Astrocytoma	+ve	-ve	+ve	-ve	I
37.	24/09	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
38.	179/09	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
39.	407/09	Anaplastic Astrocytoma	+ve	+ve	+ve	-ve	III
40.	649/09	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II
41.	700/09	Diffuse Astrocytoma	+ve	+ve	-ve	-ve	II

Astrocytomas are graded according to the WHO grading system which includes cellularity, nuclear atypia, mitosis and microvascular proliferation/necrosis as shown in the following table.

Table-9
Incidence of grades of Astrocytoma [41 / 83 cases]

Grade	No.of Cases	Percentage
I	3	7.3%
II	16	39.02%
III	14	34.1%
IV	8	19.5%

Table.9.(Fig.37) shows that most of the astrocytomas are of grade II (Fig.4) [16 cases,39.02%] followed by grade III(Fig.5) [14 cases, 34.1%]. Grade IV (Fig.6) astrocytomas, show an incidence of [8 cases 19.5%]. Least cases are seen in grade I (Fig.3) [3 cases,7.3%].

Following table No. 10 (Fig.38) shows the age wise incidence of astrocytoma. The 3 cases of grade I astrocytomas are seen in varied age group from 31-60 yrs. Grade II astrocytomas are seen in the age group of 31 -40 yrs, grade III in 31 -40yrs followed by 51-60 yrs. Grade IV astrocytomas frequently seen in the age group of 51 – 60 yrs.

Table No.10

Age wise incidence of astrocytomas

Grade	1-10Yrs	11-20 yrs	21-30Yrs	31-40 Yrs	41-50 Yrs	51-60 Yrs	61-70 Yrs
I	-	-	-	1	1	1	-
II	1	1	1	7	4	1	1
II	-	3	2	4	-	4	1
Iv	-	1	-	2	2	3	-

Table No.11
Sex wise incidence of astrocytomas

Grade	Male	Female
I	**2**	**1**
II	**7**	**9**
III	**10**	**4**
IV	**3**	**5**
Total	**22[53.6%]**	**19[46.3%]**

Table .11 illustrates the sex wise incidence of astrocytomas, This study shows a slight increased incidence in males [22 case,53.6%].

Table No -12

WHO Grading System – Meningioma [15/83 cases]

S.No	Pathology Numbers	HPE Diagnosis	Increased Cellulity	Sheeting Pattern	Increased Mitosis	Grading
1.	920/07	Conventional Meningioma	N	-ve	-ve	I
2.	1537/07	Psammomatous Meningioma (Fig.10)	N	-ve	-ve	I
3.	2232/07	Transitional Meningioma	N	-ve	-ve	I
4.	348/08	Conventional (Fig.7) Meningioma	N	-ve	-ve	I
5.	397/08	Transitional (Fig.8) Meningioma	N	-ve	-ve	I
6.	573/08	Fibrous Meningioma (Fig.9)	N	-ve	-ve	I
7.	684/08	Conventional Meningioma	N	-ve	-ve	I
8.	850/08	Conventional Meningioma	N	-ve	-ve	I
9.	1415/08	Transitional Meningioma	N	-ve	-ve	I
10.	1494/08	Anaplastic Meningioma (Fig.12)	↑	+ve	+ve	III
11.	1592/08	Transitional Meningioma	N	-ve	-ve	I
12.	1651/08	Transitional Meningioma	N	-ve	-ve	I
13.	1672/08	Fibrous Meningioma	N	-ve	-ve	I
14.	2160/08	Conventional Meningioma	N	-ve	-ve	I
15.	2236/08	Angiomatous (Fig.11) Meningioma	N	-ve	-ve	I

Likewise meningiomas are also classified according to WHO grading system as shown in the following table.12.

This table shows that 14/15 cases are in grade I with an incidence of 93.3% of varying histological patterns. One case with anaplastic features like increased cellularity, mitosis and sheeting pattern is also observed in this study.

Table No-13

AGE WISE INCIDENCE OF MENINGIOMA

S.No	Grade	1-10 Yrs	11-20 Yrs	21-30 Yrs	31-40 Yrs	41-50 Yrs	51-60 Yrs	61-70 Yrs
1.	I	-	-	2	6	4	1	1
2.	II	-	-	-	-	-	-	-
3.	III	-	-	-	1	-	-	-

Table.13 shows grade. I meningiomas are common in the age group of 31 – 40 yrs followed by 41 – 50 yrs. No cases are seen in the age group of 1 – 20 yrs.

Following table No.14 shows that meningiomas are more common in females [9 cases,60%] compared to males [6 cases, 40%].

Table No-14

SEX WISE INCIDENCE OF MENINGIOMA

S.No	Grade	Male	Female
1.	I	5	9
2.	II	-	-
3.	III	1	-
	Total	6 (40%)	9 (60%)

Following table no.14 shows that meningiomas are more common in females 9 cases 60% compared to males with 6 cases (40%). One case of anaplastic meningioma is seen in the male population.

Table No-15

WHO GRADING OF NEURAL TUMORS [7/83 CASES]

S.No	Pathology Numbers	HPE Diagnosis	Site	Mitosis	Necrosis	Grading
1.	1732/07	Neurofibroma	Not Known	-	-	I
2.	2191/07	Schwannoma	Cerebello Pontine Angle	-	-	I
3.	2776/07	Schwannoma	Cerebello Pontine Angle	-	-	I
4.	167/08	Schwannoma	Cerebello Pontine Angle	-	-	I
5.	1735/08	Ancient Schwannoma	Not Known	-	-	I
6.	2552/08	Schwannoma	Cerebello Pontine Angle	-	-	I
7.	2468/08	Schwannoma	Cerebello Pontine Angle	-	-	I

Tumors of cranial and peripheral nerves span a wide range of histological features and associated clinical characteristics. More frequently they occur in the setting of familial cancer syndromes. The tumors under this group are schwannomas, neurofibromas, perineuromas [Grade-I] and Malignant peripheral nerve sheath tumors [WHO grade III to IV]. Grading done on the basic of mitosis and necrosis. Tumors seen in our study are graded as per the above norms.

Table 15 illustrates that schwannoma is the common neural tumor seen in our study, 6 out of 7 cases with only one case of neurofibroma. The site is known in 5 cases, being the cerebellopontine angle. Site is not known in 2 cases. All cases show no necrosis or increased mitotic activity.

The below Table No.16 shows the age wise incidence of schwannoma commonly seen in the age of 31-40 yrs [3 cases] followed by 61-70 yrs [2 cases]

Table-16

AGE WISE INCIDENCE OF SCHWANNOMA

S.No	Pathology Numbers	1-10 Yrs	11-20 Yrs	21-30 Yrs	31-40 Yrs	41-50 Yrs	51-60 Yrs	61-70 Yrs
1.	2191/07	-	-	-	-	-	-	1
2.	2776/07	-	-	-	1	-	-	-
3.	167/08	-	-	-	-	1	-	-
4.	1735/08	-	-	-	1	-	-	-
5.	2252/08	-	-	-	-	-	-	1
6.	2468/08	-	-	-	1	-	-	-

Table No-17

SEX WISE INCIDENCE OF SCHWANNOMA

S.No	Pathology Numbers	Male	Female
1.	2191/07	1	-
2.	2776/07	-	1
3.	167/08	1	-
4.	1735/08	-	1
5.	2252/08	-	1
6.	2468/08	-	1
	Total	2[33%]	4[66%]

Table-17 exhibits the sex wise incidence of schwannoma. Our study shows a preponderance of females in the incidence of schwannomas [4 cases, 66%] compared to males who show an incidence of [2 cases, 33%]

CNS tumors are the second commonest occurring neoplasm in the pediatric population, next to hematological malignancies Embryonal tumors are the commonest CNS neoplasms in children. In our study 11 cases are in the pediatric

age group giving an incidence of 13.2% of all CNS neoplasms. The various CNS neoplasms seen in our study are exhibited in table No:18.

Table No-18

INCIDENCE OF CNS NEOPLASMS IN PEDIATRIC POPULATION

S.No	Pathology Numbers	HPE Diagnosis	Grade
1.	133/07	Medulloblastoma (Fig.14)	IV
2.	1485/07	Rhabdomyosarcoma/Lymphoma	-
3.	2613/07	Oligodendroglioma (Fig17)	II
4.	2665/07	Choroid Plexus Papilloma (Fig16)	I
5.	57/08	Craniopharyngioma (Fig15)	I
6.	237/08	Craniopharyngioma	I
7.	1768/08	Medulloblastoma	IV
8.	2314/08	Medulloblastoma	IV
9.	3148/08	Medulloblastoma	IV
10.	179/09	Astrocytoma	II
11.	458/09	Small Round Blue Cell Tumour	-

Table 18 (Fig39) shows that medulloblastoma is the commonest CNS neoplasm in pediatric population in our study [4 cases, 36%] followed by craniopharyngioma [2 cases-18%]. One case each of oligodendroglioma, choroid plexus papilloma and astrocytoma are seen. 2 doubtful cases diagnosed as Small Blue Round cell tumor and Rhabdomyosarcoma / lymphoma are seen for which immunohistochemistry is done for confirmation.

Table No-19
SEX WISE INCIDENCE OF CNS NEOPLASM ACCORDING TO WHO GRADE IN PEDIATRIC POPULATION

Grade	Male	Female
I	-	3
II	-	2
III	-	-
IV	2	2

Table no 19 (Fig40) shows that pediatric CNS neoplasms are commonly seen in female children 7 out of 11 cases [63.6%] compared to male who show an incidence of 2 cases [18.2%].

Metastatic tumors are neoplasms involving the CNS but are discontinuous with primary systemic neoplasms. Intracranial metastasis is most frequent in brain and dura. Origin of brain metastasis is mostly from respiratory tract, breast and skin. The metastatic tumors seen in our study with probable site of primary is illustrated in table no:20.

Table No-20
INCIDENCE OF METASTATIC TUMORS WITH PROBABLE SITE OF PRIMARY [5/83 CASES]

S.No	Pathology Numbers	Age/Sex	HPE Diagnosis	Probable Site
1.	2532/07	27/F	Choriocarcinoma (Fig18)	Uterus
2.	292/08	50/F	Adenocarcinoma (Fig19)	Breast
3.	52/08	27/F	Carcinoma (Fig20)	Not Known
4.	2469/08	45/F	Follicular Carcinoma (Fig.21)	Thyroid
5.	2637/08	40/F	Adenocarcinoma	Not Known

Table 20 shows that 5 cases of metastasis are seen in our study with an incidence of 6.03% All the cases are seen in females with site of primary known in 3 cases, sites being breast uterus and thyroid. The site is not known in 2 cases.

Table 21

Immunohistochemical analysis of CNS tumors [4 cases]

Immunohistochemical analysis is done for 4 cases in our study where diagnosis based only on light microscopy was difficult. The results are illustrated in the below table.

S.No	Pathology Nos	HPE Diagnosis	GFAP	Synaptophysin	Desmin	CD 40	CD68	Final Diagnosis
1.	2172/07	Glioblastoma Multiforme small cell variant	-ve	+ve	ND	ND	ND	Primitive Neuroectodermal tumor (Fig24,25)
2.	1485/07	RMS/Lymphoma/Malignant Histiocytosis	ND	ND	-ve	-ve	+ve	Malignant Histiocytosis (Fig26,27)
3.	323./08	Gliosareoma / Lymphoma	+ve	ND	ND	-ve	ND	Gliosarcoma (Fig28,29,30)
4.	458/09	Small round Blue cell Tumors	-ve	+ve	ND	ND	ND	Primitive Neuroectodermal tumor (Fig31,32)

ND : Not done

GFAP: Glial Fibrillary Acidic Protein

Immunohistochemical analysis of 4 cases posing diagnostic problems is done with a panel of antibodies consisting of GFAP, Synaptophysin, desmin, CD40 and CD 68 . GFAP found positive in 1 case and a final diagnosis of Gliosarcoma given. Synaptophysin found positive in 2 cases and a diagnosis of Primitive Neuroectodermal tumor made in both. CD 68 found positive in 1 case where a panel of other 2 markers were also used (Desmin and CD 40), left with the diagnosis of Malignant Histiocytosis.

CONCLUSION

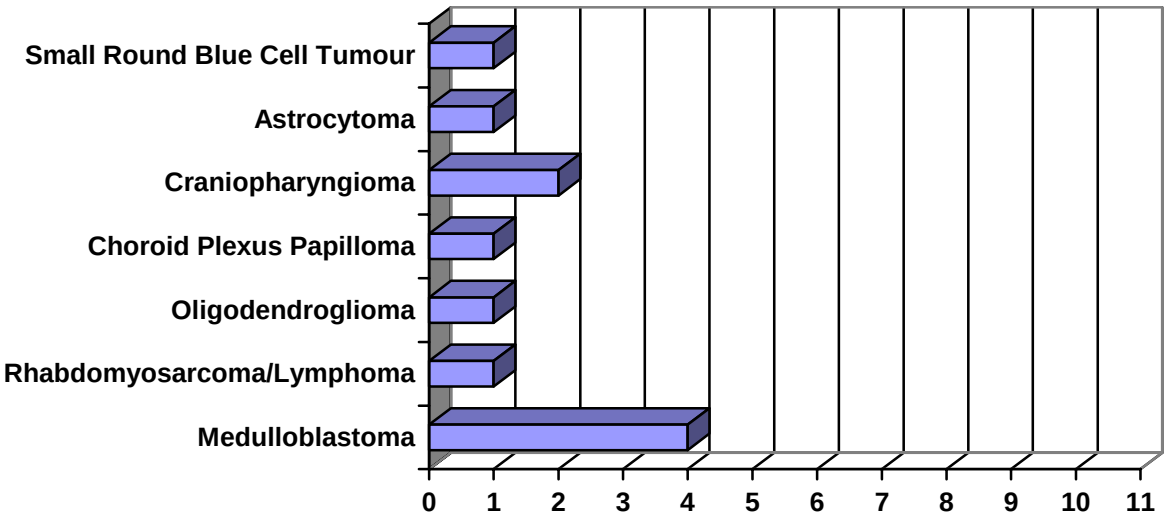
In the present prospective study of 83 central nervous system neoplasms evaluated with clinical, histopathological, histochemistry and immunohistochemistry, the following conclusions are made and presented.

1. The incidence of CNS neoplasms is 9.97%.
2. High incidence of CNS neoplasms is seen in the 3rd and 4th decade with slight female predominance.
3. Primary CNS tumors are seen supratentorially in adults and in children it occurs infratentorially.
4. Astrocytomas constitute the most common CNS tumor.
5. Grading of astrocytomas by WHO norms reveal grade II pattern as the commonest.
6. Meningiomas and Schwannomas constitute the next common CNS tumor.
7. In the pediatric age group, grade IV neoplasms are common, medulloblastoma being the commonest malignant tumor.
8. Metastatic tumors to the brain are commonly seen in females in the 2nd to 4th decade, probable sites of primary being uterus, breast and thyroid.
9. Special stains help in the diagnosis of CNS tumors to a limited extent.
10. In doubtful cases immunohistochemical markers provide a valuable tool in arriving at a final diagnosis.

Immunohistochemistry is one of the most important tools of diagnostic histopathology. But now more stress is on finding tumor marker of prognostic significance. Survival in astrocytic gliomas is closely related to WHO tumor grade. Within tumor grade, especially in grade II and III tumors, the clinical course is variable and can hardly be predicted by histological criteria. Neovascularisation is a neuropathological hallmark in high grade gliomas and angiogenic factors may play an important role in malignant tumor progression.

Recently there has been conjecture that primary brain tumor incidence is increasing. This apparent rise is most likely caused by factors such as better diagnostic procedures and improved access to medical care. The future immunohistochemistry is aimed at not only the diagnosis and prognostication of the tumors but also being able to comment upon the probable response to various adjuvant agents.

INCIDENCE OF CNS NEOPLASMS IN PEDIATRIC POPULATION



WHO Classification of Tumors of the Nervous System

Neurofibroma 9540/0

Plexiform 9550/0

Perineurioma 9540/0

Intraneural perineurioma 9571/0
Soft tissue perineurioma 9571/0

Malignant peripheral 'Nerve sheath tumor (MPNST) 9540/3

Epithelioid 9540/3
MPNST with divergent

Mesenchymal and / or epithelial

differentiation 9540/3
Melanotic 9540/3

Melanotic psammomatous 9540/3

TUMORS OF THE MENINGES

Tumors of meningothelial cells

Meningioma 9530/0

Meningothelial 9531/0

Fibrous (fibroblastic) 9532/0

Transitional (mixed) 9537/0

Psammomatous 9533/0
Angiomatous 9534/0
Microcystic 9530/0
Secretory 9530/0

Lymphoplasmacyte-rich 9530/0

Metaplastic 9530/0

Clear cell 9538/1
Chordoid 9538/1
Atypical 9539/1
Papillary 9538/3
Rhabdoid 9538/3
Anaplastic meningioma 9530/3

Mesenchymal, non-meningothelial tumors

Lipoma 8850/0

Angiolipoma 8861/0
Hibernoma 8880/0
Liposarcoma (intracranial) 8850/3

Solitary fibrous tumors 8815/0

Fibrosarcoma 8810/3

Malignant fibrous histiocytoma 8830/3

Leiomyoma 8890/0
Leiomyosarcoma 8890/3
Rhabdomyoma 8900/0
Rhabdomyosarcoma 8900/3
Chondroma 9220/0
Chondrosarcoma 9220/3

Osteoma 9180/0

Osteosarcoma 9180/3
Osteochondroma 9210/0

Haemangioma 9120/0

Epithelioid haemangioendothelioma 9133/1

Haemangiopericytoma 9150/1
Angiosarcoma 9120/3

Kaposi sarcoma 9140/3

Primary melanocyte lesions

Diffuse melanocytosis 8728/0
Melanocytoma 8728/1

Malignant melanoma 8720/0

Meningeal melanomatosis 8728/3

Tumors of uncertain histogenesis Haemangioblastoma 9161/1

LYMPHOMAS AND HAEMOPOIETIC NEOPLASMS

Malignant lymphomas 9590/3
Plasmacytoma 9731/3
Granulocytic sarcoma 9930/3

GERM CELL TUMORS

Germinoma 9064/3
Embryonal carcinoma 9070/3
Yolk sac tumors 9071/3
Choriocarcinoma 9100/3
Teratoma 9080/1
Mature 9080/0
Immature 9080/3
Teratoma with malignant
Transformation 9084/3
Mixed germ cell tumors 9085/3

TUMORS OF THE SELLAR REGION

Craniopharyngioma ' 9350/1
Adamantinomatous 9351/1
Papillary 9352/1
Granular cell tumor 9582/0

Adopted from World Health Organization classification of tumors pathology & genetic tumors of the nervous system 2000 edited by Paul kleihues & Webster K. Cavenee

WHO Classification of Tumors of the Nervous System

Tumors of Neuroepithelial Tissue

Astrocytic tumors

Diffuse astrocytoma	9400/3
Fibrillary astrocytoma	9420/3
Protoplasmic astrocytoma	9410/3
Gemistocytic astrocytoma	9411/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9411/3
Gliosarcoma	9442/3
Pilocytic astrocytoma	9421/1
Pleomorphic xanthoastrocytoma	9424/3
Subependymal giant cell Astrocytoma	9384/1

Oligodendroglial tumors

Oligodendroglioma	9450/3
Anaplastic Oligodendroglioma	9451/3

Mixed gliomas

Oligoastrocytoma	9382/3
.Anaplastic oligoastrocytoma	9382/3

Ependymal tumors

Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
Myxopapillary ependymoma	9394/1
Subependymoma	9383/1

Choroid plexus tumors

Choroid plexus papilloma	9390/0
Choroidplexus carcinoma	9390/3

Glial tumors of uncertain origin

Astroblastoma	9430/3
Gliomatosis cerebri	9381/3
Chordoid glioma of the3rd ventricle	9444/1

Neuronal and mixed neuronal-Glial tumors

Gangliocytoma	9492/
Dysplastic gangliocytoma of cerebellum(Lhermitte-Duclos)	9493/
9493/Desmoplastic infantile Astrocytoma / ganglioglioma	9412/
Dysembryoplastic neuroepithelial tumor	9413/
Ganglioglioma	9505/
Anaplastic ganglioglioma	9505/
Central neurocytoma	9506/
Cerebellar liponeurocytoma	9506/
Paraganglioma of the filum terminale	8680/

Neuroblastic tumors

Olfactory neuroblastoma (Aesthesioneuroblastoma)	9522/
Olfactory neuroepithelioma	9523/
Neuroblastomas of the adrenal gland and sympathetic nervous system	9500/

Pineal parenchymal tumors

Pineocytoma	9361/
Pineoblastoma	9362/
Pineal parenchymal tumor of Intermediate differentiation	9362/

Embryonal tumors

Medulloepithelioma	9501/
Ependymoblastoma	9392/
Medulloblastoma	9470/
Desmoplastic medulloblastoma	9471/
Large cell medulloblastoma	9474/
Medullomyoblastoma	9472/
Melanotic medulloblastoma	9470/
Supratentorial primitive Neuroectodermal tumor (PNET)	9473/
Neuroblastoma	9500/
Ganglioneuroblastoma	9490/
Atypical teratoid / Rhabdoidal tumor	9508/

Tumors of Peripheral Nerves

Schwannoma (Neurilemmoma, Neurinoma)	9560/0
Cellular	9560/0
Plexiform	9560/0
Melanotic	0560/0

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